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Neovascularization After Great Saphenous Vein Ablation

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Objective. To determine the prevalence, distribution, and flow characteristics of intraluminal neovascularization in patients undergoing great saphenous vein (GSV) endovenous laser (EVL) or radiofrequency ablation (RFA).

Methods. Duplex ultrasound (DU) was performed in patients undergoing EVLT or RFA before, during, and after their procedures. Follow-up included assessment for deep venous thrombosis and obliteration. When new vessels were identified, the source, extent, direction, and location of flow were noted. Flow channel diameters were measured and the resistivity index (RI) was used to characterize the flow patterns.

Results. A total of 102 venous ablations were performed of which 46 were RFA, and 56 EVLT. Arterio-venous fistulae (AVF) were found in five patients that were not identified by DU prior to intervention. Involved segments had variable length and multiple channels (mean diameter 2.2 mm). No patient had local or systemic symptoms related to the AVF. The mean RI was 0.42, consistent with an AVF. The perivenous arteries feeding the AVF had enhanced flow but a significantly higher RI (0.63, $p < 0.001$).

Conclusion. Multiple small vessels were found directly adjacent to the involved vein segments forming small AVF within the obliterated vein. The prevalence of AVF in the ablated GSV was 5%. This process may be responsible for recanalization or recurrence after endovenous ablation procedures.

Keywords: Neovascularization; Thrombus; Laser; Radiofrequency ablation; Great saphenous vein; Arteriovenous fistula.

Introduction

Endovenous laser (EVL) or radiofrequency ablation (RFA) of veins has become an increasingly employed modality in the treatment of chronic venous disease (CVD). Duplex ultrasound (DU) is frequently performed before, during, and after these procedures, allowing the natural history of thermal venous obliteration to be studied. We have observed new vessel formation in patients with acute venous thrombosis.¹ Such vessels have been described in animal models.² A similar process was noted in our patients that underwent venous obliteration. This study was designed to determine the prevalence, distribution, extent, and flow characteristics of this phenomenon in patients undergoing RFA or EVLT.

Methods

DU was performed in patients undergoing EVLT or RFA prior to, during, and 1-week after their great

saphenous vein (GSV) ablation procedures. A small number of patients underwent DU at a month because of symptoms in the treated limb or being unable to make their first post-ablation appointment. Patients with a history of previous surgery, trauma, sclerotherapy, or venous thrombosis were excluded. Linear array multifrequency transducers 4–7, 4–8 and 5–12 MHz were used with HDI 5000 and I22 scanners (Philips Medical Systems, Bothell Washington). All endovenous ablations were performed with sparing of the saphenofemoral junction. For this reason, the catheter was always placed at least 1 cm distal to the union of the epigastric vein and the GSV.

Post-venous ablation patients were examined for deep venous thrombosis (DVT) and for successful obliteration of the treated veins. Compression, color flow imaging, and Doppler examination of the superficial and deep veins were used to determine patency. Particular attention was placed for extension of thrombus from the ablated segment to the common femoral vein. The entire length of the GSV was imaged with low-flow settings (pulse-repetition frequency < 1500 Hz and color-gain > 70) to detect recanalization, new vessel formation and to facilitate visualization of adjacent small vessels. The color gain was decreased and the pulse-repetition frequency increased in vessels with high flow.

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When blood vessels were detected within the obliterated vein a detailed examination was performed to identify the source, extent, direction, and location of flow. The appearance and flow characteristics of adjacent arteries were also evaluated. Flow channel diameters were measured either in B-mode or with color flow. The peak systolic (PSV) and end-diastolic velocities (EDV) were recorded and the resistivity index (RI) was used to characterize the flow pattern using the formula (PSV-EDV)/PSV.

Descriptive statistics were used for the analysis. Fisher's exact test was used to compare the difference in prevalence of AVF in RFA and EVLT procedures. Unpaired *t*-test was used to compare RI values.

Results

A total of 102 venous ablations were performed of which 46 were RFA and 56 EVLT. After ablation, 5 GSVs in five patients had intrathrombus neovascularization (three were right and two were left) (Table 1). There were four females and one male with a mean age of 47.8 years ranging from 31 to 57. The flow patterns of these vessels are shown in Fig. 1a and b. They were fed by small arteries around the GSV that penetrated the venous wall in all cases (Fig. 1c). The length of the involved segments measured 2, 4, 5, 7 cm and the entire ablated GSV from knee to groin in the last patient. All patients had multiple channels in the thrombus coursing in different directions (perpendicular, oblique and parallel to the vein wall). There were at least two entry points from surrounding arteries that were feeding the intraluminal channels. No patient had local or systemic symptoms related to the identified intrathrombus vessels. These vessels were not present prior to intervention. The small arteries adjacent to the ablated veins had significantly increased PSV and EDV compared to those prior to ablation. Also, the reverse flow component was absent post-ablation. The intra-thrombus vessels had a significantly lower RI than the adjacent arteries Fig. 1d (RI \pm SD; 0.63 ± 0.01 vs 0.42 ± 0.07 , $p < 0.001$). The mean diameter of these channels was 2.22 mm (range 1–5.6 mm). The flow characteristics of the intrathrombus channels were typical of arteriovenous

fistulae (AVF), demonstrating pulsatile low resistance flow with a significant diastolic component. Two patients (2%) developed short extensions of the GSV thrombus into the common femoral vein. Neither of these had AVF at the extension site or in the ablated GSV.

Discussion

In our study of post ablation venous segments, we identified multiple small vessels with arterial signals directly adjacent to the involved vein segments forming multiple small AVF within the obliterated vein. Penetrating vessels were identified in all cases, and flow occurred through several channels within the obliterated vein. The flow signals in the thrombus were characterized as AVF because they had a high diastolic flow and a low RI.

The mechanisms of thrombosis and vein injury with thermal ablation are different from those found in *de novo* DVT formation. RFA is thought to ablate veins through formation and resorption of thrombus, intimal injury, shrinkage, and denaturation of the vein wall.³ EVLT is thought to cause vein ablation through thrombosis and thermal injury.^{4,5} One recent study found a high prevalence of 'small vessel networks' and 'clusters of arteries and veins' adjacent to recanalized vein segments after radiofrequency ablation.⁶ We confirmed these observations as enhanced perivenous flow was found. Such enhanced flow has been described in patients with acute and chronic inflammation.^{7,8}

We have shown previously that this phenomenon occurs in acute thrombosis of both superficial and deep veins.¹ EVLT, which produces more thrombus than RFA, has a higher incidence of AVF formation. However, due to the low prevalence of AVF formation in both procedures the difference was not significant. Venous thrombosis has been shown to have an inflammatory component, which is well described in animal models.^{9,10} Inflammatory mediators and infiltrates such as monocytes, neutrophils and cytokines play an integral role in thrombus remodeling.^{2,11–13} Positive staining of various endothelial markers has been demonstrated during thrombus recanalization.²

We found only two cases with DVT within a week after the ablation. This prevalence is consistent with the findings of most published series. No AVF was found in either of these cases in the ablated vein or in the thrombus extending into the common femoral vein. Both patients were asymptomatic and were placed on low molecular weight heparin. A subsequent scan in both cases revealed no thrombus

Table 1. Incidence of AVF in endovenous ablation

Endovenous ablation technique	# AVF	Procedures	%
Radio frequency	1	46	2.2
Laser	4	56	7.1
Total	5	102	4.9

$p = 0.64$.

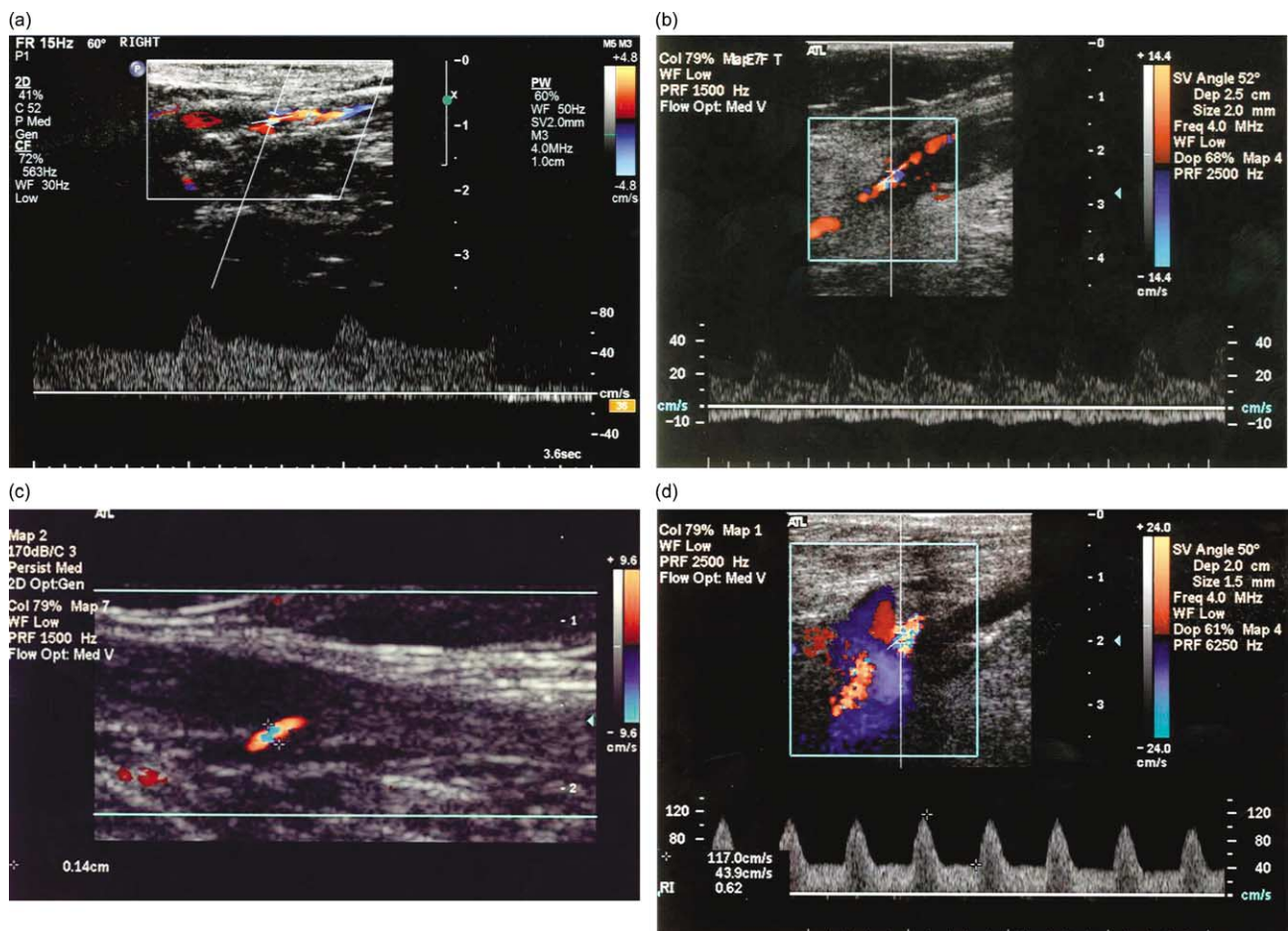


Fig. 1. Flow characteristics from patients with endovenous ablation procedures. (a) AVF flow in the upper thigh of GSV from a 53-year-old male who had an RFA 4 weeks earlier. (b) AVF in the upper thigh of a 57-year-old female who had an EVLT 1 week earlier. Both cases had enhanced flow within the thrombus and RI of 0.44 and 0.5, respectively. (c) A surrounding vessel penetrates the far wall of the GSV to feed intrathrombus vessels. It was measured at the entry point crossing the adventitia of the GSV. It clearly demonstrates the wall defect at that level which matches the diameter of the feeding artery. (d) Enhanced perivenous arterial flow near the SFJ in a 59-year-old female 1-week post EVLT. Like in most patients with endovenous ablation no AVF was found in this case. The RI was 0.62, which is higher than the AVF cases. Such vessels were seen after the procedure due to the local inflammation produced from thermal injury.

extension or AVF formation. Thrombus extension may not influence AVF formation or alternatively AVF development could inhibit propagation. Clearly more work is needed to define these phenomena.

The AVF formation found may be responsible for recanalization of the ablated venous segments. This may be related to the amount of thrombus produced during ablation and to the intensity of the inflammatory response in different people. It is possible that such vessels may develop in most, if not all, ablation procedures. However, these vessels could be too small to be detected by ultrasound. Animal models and histopathologic studies would help identify the etiology and potential implications of this phenomenon. At the present time, the clinical significance of this finding remains unclear.

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